

Renal replacement therapy in Ireland – the Belfast experience

Based on the 2nd J Creery Ferguson Memorial Lecture of the Royal College of Physicians of Ireland on the occasion of the bicentenary of the Royal Victoria Hospital – 7th March 1997

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“Science is like a web, growing by interactions which reach out in time and space”.¹ Such interactions between individuals working in science and medicine have contributed to the jigsaw of knowledge, and these human linkages were as powerful then in their effect as the Internet may become one day.

Dr John Creery Ferguson provides a good example of the interactions and links between Belfast and Dublin. Born in Tandragee in 1802, he was the son of Dr Thomas Ferguson who later practised in Dublin.² After graduating in Arts in Dublin University in 1823, John Creery Ferguson studied medicine in Edinburgh where he graduated in 1825. Fellow graduates were Stokes and Corrigan. He then studied in Paris with Kergaradec and Laennec. Kergaradec had already used the stethoscope to auscultate the human pregnant abdomen, and soon after his return to Dublin in 1827 Ferguson heard the human fetal heart, the first to do so in the British Isles. In 1827 he was granted the license and, in 1829 the Fellowship of the King and Queen's College of Physicians. He was appointed Professor of Medicine in the Queen's College, Belfast in 1846 and spent the remainder of his life there. He was the first President of the Ulster Medical Society in 1862. He died in 1865.

Until the end of the second world war, the hospital ward was the kingdom of a senior doctor. In the larger teaching hospitals working alongside the pre-eminent consultant was often a younger colleague, already well qualified, who shared the use of beds, outpatient departments and laboratory facilities, if there were any. The practical work of patient care was done to a large extent by junior doctors in training, differing in experience and

skill. Patient care not requiring medically trained personnel was carried out by nursing staff at varying levels of proficiency.

As a student trained during the war, when newly qualified doctors very soon went off to the Forces, I revelled in being a resident pupil. It fell to us to write the clinical history of the newly admitted patients. Proficiency in taking blood samples, giving injections, performing lumbar punctures, aspirating pleural effusions and collections of fluid elsewhere in the body, and the administration of anaesthesia for minor procedures was acquired while a student. The increased confidence in approaching patients is sometimes derided as the “bedside manner”, but at its best it is a real social skill to be acquired, which greatly eases contact between patients and doctors. We had the task of testing routine early morning admission urine samples. In the Royal Victoria Hospital students carried out blood sugar and blood urea estimations. It is awesome to remember that decisions on the treatment of patients were actually based on the tests we carried out in the side ward. The flame photometer was still an esoteric research tool, body fluid electrolytes were not yet measured for clinical purposes.

By the early 1950's in Belfast some special areas of expertise had already been recognised, within medicine – cardiology, mental diseases, neurology and dermatology; in surgery – orthopaedics, otorhinolaryngology and ophthalmic surgery. At the end of the war even neurosurgery was carried out by a general surgeon, Mr Barney Purce. Urology had begun to develop, but in this field Dublin was more advanced than Belfast. A supporter of these developments was Professor John Henry Biggart, Dean of the Faculty of

Medicine in the Queen's University from 1943 until 1970. His lectures were always interesting and stimulating; with his personal magnetism they have remained in my memory. His message was that a sound understanding of pathology was not only the key to understanding human diseases, but also the foundation of training for the aspiring clinician. Remembering this dictum, many of us made our way to the Institute of Pathology.

This was the scene in which early attempts at organ replacement occurred. Replacement of renal function was the earliest and still is, by far, the most widely used form of organ replacement therapy. Before the war the physiology of the kidneys and diseases of the urinary tract were poorly understood. Although it was appreciated that renal tubular function controls to a large extent the acid base equilibrium in the body, urine was regarded mainly as a means of excretion of excess water and electrolytes. Nothing at all was known about the important endocrine function of the kidneys.

Effective treatment of kidney failure dates from the invention during World War II of the first workable artificial kidney by Dr Willem Kolff (Fig. 1) in Klampen, a small town in occupied Holland. He demonstrated that when the kidneys have failed, the waste products of metabolism could be removed from the bloodstream, and that clinical improvement rapidly followed. Moreover, repeated treatment enabled many patients whose

kidneys had failed acutely to be kept alive long enough for kidney function to recover. The idea of removing toxic substances from the bloodstream was not new, but Kolff devised the first practical equipment for this purpose, and the first evidence that acute renal failure need not be irreversible.

During Kolff's treatment the patient's blood was passed from a cannula placed in the radial artery into a long tube of cellophane wound around a supporting horizontal drum. The drum rotated on a spindle so that the blood-filled tubing was repeatedly bathed in a tank containing dialysis fluid. The cleansed blood was then returned to the patient through another cannula inserted into an adjacent large vein on the same limb, the process being repeated until the biochemical abnormalities were considerably ameliorated. The blood was prevented from clotting by repeated injections of heparin into the blood circuit. Kolff reported his work in 1944,³ and subsequently gave artificial



Fig 1. Willen Kolff and the author, 1966.

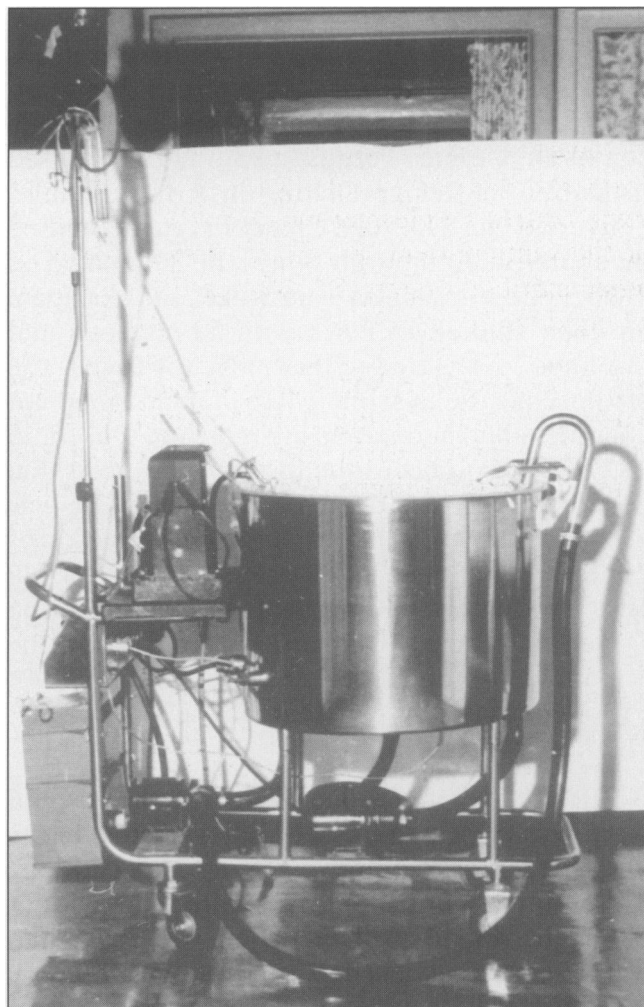


Fig 2. Kolff's "Twin Coil" artificial kidney, in use in Belfast 1959-1970.

kidneys to Hammersmith Hospital in London, Mount Sinai Hospital in New York and the Royal Victoria Hospital in Montreal, all of which reported successful treatments. Sadly, the kidney he gave to Amsterdam was never used. These reports, as well as leading to the setting up of new artificial kidney units over the world, stimulated great interest in the human kidney, its function and its diseases. Kolff went on to devise an improved twin coil artificial kidney, where a very large surface area was provided, the stream of blood issuing from the patient being divided into two, to supply two tubes (Fig. 2). This design could be manufactured sterile and ready for use – the first disposable artificial kidney. In all coil dialysers (several modifications appeared later) the dialysis fluid is pumped around the blood filled dialysis tube, instead of the tubing being rotated in a stationary bath of fluid. The coil is supported in a container, the fluid is pumped through the coil and splashes back into the bath to be re-circulated. About the mid 1960's Kolff's team with the commercial support of the Dow Corning Company jointly developed the capillary kidney. In this blood is pumped through enormous numbers of capillary tubes spun of dialysis membrane, around which the fluid is pumped. Although intended to be a disposable kidney, in some centres it is cleaned and re-used for treatment of the same patient. Kolff went on to work on other artificial organs. By 1966 he had produced an artificial heart.

My experience as a house surgeon in 1947, with Mr Cecil Woodside (Fig. 3) in the Royal Victoria Hospital, proved to be the foundation of my career in renal medicine. Woodside had achieved international recognition for his work on stone disease, and was to have been awarded a medal at the International Congress of Urology in Barcelona in 1939, which was cancelled because of the outbreak of war. There were always patients in his wards undergoing investigation and surgery for renal stones. He urged me to consider a career based on research into causation of stone disease. However paediatrics had always attracted me, and after a post as house physician in the Royal Belfast Hospital for Sick Children, I went to Professor Biggart's department to work for the degree of MD. This achieved, I went to see the Professor of Paediatrics hoping to be accepted as a trainee in his specialty. His immediate answer was "No!" I was a woman and married, there were plenty of young men aiming for his specialty.



Fig 3. Cecil J A Woodside, FRCS (1897-1955): Senior Surgeon, Royal Victoria Hospital, and first Chairman of the Northern Ireland Hospitals' Authority.

I was bitterly disappointed as I had won the Gold Medal in Diseases of Childhood in the final MB examination and two postgraduate scholarships in the subject. My husband suggested that I should learn about biochemistry, but the Professor of Biochemistry would accept me only on condition that I was prepared to work as a research student for a PhD. Three years later, now with the degrees of both MD and PhD, I seemed little better equipped for the hospital job rat race.

Mr Woodside, maintaining his interest in me, had a good suggestion – Dr Graham Bull who had recently come to Belfast as the first full-time Professor of Medicine (Fig. 4), might have a place for me. Quite reasonably, after hearing my story, Professor Bull said that while there was a post as lecturer in medicine available, I had not worked in clinical medicine for nearly five years, and was not a suitable candidate. However, he suggested that I might be a suitable candidate for a personal grant from the MRC, if I could produce a research topic. Bull was just about to set up a laboratory for the Department of Medicine, and I suppose saw me as someone with laboratory experience who could help choose new apparatus and organise it. He said "Go and bash the books in the library and come back with a detailed



Fig 4. Professor (later Sir) Graham McG Bull, MD, FRCP (1918-1987): first full-time professor of Medicine, The Queen's University of Belfast.

project". Amazingly this resulted in a personal grant from the MRC which supported me for five years.

In 1948 Graham Bull had arrived at Hammersmith Hospital in London from Cape Town. The team there, including Malcolm Milne, Russell Fraser, Joe Yucas and Jan Borst began to use Kolff's rotating drum kidney. By Bull's accounts dialysis treatment with the original model was a formidable task. It took several hours to prepare the apparatus, and six hours for the treatment. The patient often developed rigors and even convulsions. In the hope of avoiding its use, he and his colleagues developed the so-called "conservative treatment".⁴ This was based on careful control of fluid and electrolyte balance, provision of calories as pure carbohydrate and fat to spare breakdown of body tissues with its resultant production of nitrogen and potassium. The regimen later became famous as the Bull-Borst diet. In theory the treatment could be used anywhere and doubtless saved many lives world-wide. Many patients

with acute renal failure recovered their kidney function within a week or 10 days, and conservative management was sufficient to save them, but for those with more severe kidney failure, it was not sufficient. Moreover the diet of glucose or lactose and oil further increased the patients' nausea, and they developed sore mouths. They became very thirsty, but if they were totally anuric fluid intake had to be restricted to 400 mls daily. Cardiac arrest from a high potassium level was a serious risk.

One day in 1958, Professor Bull called me to his room. He had with him Mr John Megaw (Fig. 5) Consultant Surgeon at the Belfast City Hospital. Mr Megaw saw specialisation in urology beckoning, but was hesitant about giving up general surgery – in fact he never did so. The event which led to his visit was a patient we had just treated in the Royal Belfast Hospital for Sick Children. He was a boy seriously injured in a road accident who developed acute renal failure. Conservative treatment appeared to be insufficient, and he was transferred to Hammersmith Hospital in the belief that without artificial kidney treatment he would die. Ironically, he began to produce urine during the journey to the Hammersmith. This event led to questions being asked in the Stormont Parliament, followed by a statement urging that Northern Ireland should have an artificial kidney. Megaw saw this as an opportunity to enhance the image of the Belfast City Hospital, hence his visit to Bull. Until Megaw's momentous visit to him in 1958, Bull had maintained that most patients with acute renal failure would recover with conservative treatment, and that the population of Northern Ireland was not big enough to justify an artificial kidney. Megaw wanted to set up an artificial kidney unit at the Belfast City Hospital and was looking for someone with suitable training. Bull knew that I desperately wanted a post which gave more contact with patients – I already ran a special clinic for patients with kidney stones. I had never seen an artificial kidney and he knew this, but silenced my objections, explaining to Megaw how my training and experience suited me for the project.

Some weeks later, with Megaw and John Storey (head of the firm which supplied hospital equipment to the Northern Ireland Hospitals Authority), I set off on visits to see the two models of artificial kidney then available. In Leeds General Infirmary Dr Frank Parsons



Fig 5. John Megaw, FRCS (1913-1971): Senior Surgeon, Belfast City Hospital, whose plan it was that an artificial kidney service should be situated there.

demonstrated his rotating drum kidney. He reiterated the problems described by Bull, and I became more and more disenchanted with the whole idea. We then visited the RAF Renal Unit at Halton, headed by Dr Ralph Jackson (later Air Vice-Marshal Sir Ralph Jackson) who showed us the twin coil kidney. This appeared to be much simpler in use and very efficient. Jackson assured me that my laboratory background was a good preparation. What I needed was a suitable isolation room, the twin coil artificial kidney, and a technician to assist me in preparing the equipment and weighing out chemicals. He could arrange for me to stay for a short period in Halton to see how it was set up and used. He advised that I should wait until our equipment arrived, and I had had time to do mock set-ups before the visit.

The twin coil artificial kidney was ordered and plans were made to remodel Ward 9 in the main block of the Belfast City Hospital to include a two-bed renal unit. A technician, Maurice Bingham, was recruited from the biochemistry laboratory. The artificial kidney arrived in early June 1959, but Ward 9 was not yet ready and we were given a small storeroom in which to store it.

It happened that a refresher course was being held in the City Hospital two days later. Mr Megaw insisted that I should set up the artificial kidney and demonstrate it to the general practitioners. I had seen a twin coil kidney once – Maurice Bingham had never seen one. We read the accompanying booklet and proceeded to set it up, using red ink to mimic the blood circuit. Mr Megaw and the assembled family doctors seemed suitably impressed.

Meanwhile Dr Haskel Eliahou from Israel, who was just finishing a year's attachment to Professor Bull's ward, came to ask me to let him see the new kidney in action before he returned home. We persuaded Mr Richard Welbourn, Senior Lecturer in Surgery, to ligate the ureters of a dog, which after 48 hours became profoundly uraemic. The first haemodialysis in Northern Ireland was carried out in the animal theatre in the Department of Surgery. We managed to treat the dog with a short dialysis, enough to demonstrate a considerable reduction in the blood urea concentration. Dr Eliahou returned to Israel where he set up the Renal Unit in Tel Aviv, and later became a world expert in the treatment of acute renal failure.

I was now ready to visit Halton and see how dialysis should be carried out. However, the following week an elderly man was admitted in uraemia due to prostatism. He was semi-comatose with a blood urea of over 600 mg/100 ml. Megaw demanded that I should treat him by dialysis. Maurice and I set up the twin coil kidney in Ava 2 theatre in the children's department of the Belfast City Hospital and Eileen Martin, the technician in the Department of Medicine Laboratory, weighed out three sets of chemicals to make up three batches of dialysis fluid. On 22nd June 1959, in fear and trepidation we treated our first patient. Unfortunately after immediate improvement he died within a week of a stroke.

From then on we were in business. Still without our accommodation, our headquarters a storeroom, we became a travelling dialysis service. The hospital van took us and our equipment to the patient, most frequently in the Royal Victoria Hospital. We dialysed patients there and in other Belfast hospitals many times. There were always problems, plugs did not fit and there were difficulties with the water supply. Our second patient recovered from post-natal renal failure after 36 days of virtual anuria. When I last saw her, more than 20 years later, she had

normal renal function. She had undergone another successful uneventful pregnancy. Another early patient who developed acute renal failure following an incompatible blood transfusion presented a problem in treatment. It was necessary to cross-match about 250 units of blood in order to find the 15 units of compatible blood needed to prime the dialyser for her several treatments. She too made a long-term complete recovery – and so I never got to Halton to see how haemodialysis should be done.



Fig 6. Anthony Walsh, FRCS (1922-1997): dialysis surgeon and later first transplant surgeon at Jervis Street Hospital, Dublin.

At this point during a family holiday we spent a night in Dublin. I learned that Jervis Street Hospital had recently obtained an artificial kidney, which was operated by a Dr Joe Woodcock. They had done their first haemodialysis in 1958, and were now at about the same stage as ourselves. A few months later the Dublin urologist, Anthony Walsh (Fig. 6) arranged a meeting with Billy O'Dwyer (Fig. 7) the physician of the Jervis Street team. Late that Saturday night Tony Walsh was called in to insert cannulae for a two year old girl with undiagnosed renal failure. I remember that she was as white as a sheet and that her bladder was empty. It was difficult to maintain her blood pressure during dialysis, despite much transfusion, and we thought she might not survive. However, she recovered after several more

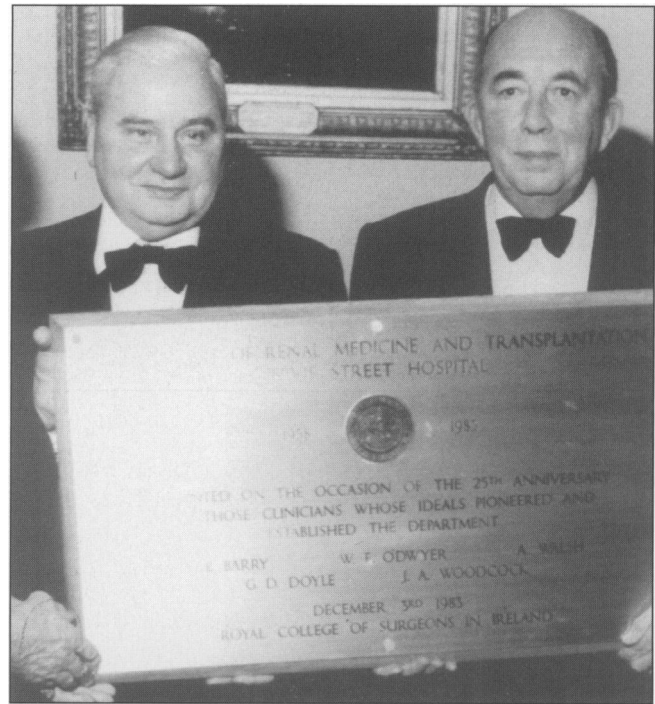


Fig 7. William O'Dwyer, MD, FRCPI (1916-1997), consultant physician, Joseph Woodcock, Woodcock, FRCPI (1918-1997): who collaborated with Anthony Walsh at Jervis Street Hospital, Dublin, in setting up the haemodialysis and renal transplantation service there.

treatments over the next ten days. For all three of us it was a first encounter with the acute haemolytic uraemic syndrome which recently had been described. That episode was the beginning of life-long friendships with Billy, Tony and their wives. In 1961 when the birth of my youngest child was imminent, I was still working single-handed. Billy telephoned from Dublin to say he and their team would hold themselves on call should dialysis be needed, while I had maternity leave. Maternity leave was three weeks beginning on the day on which my son was born.

In 1960 we moved into the new two-bed dialysis unit in the Belfast City Hospital. That year Maurice Bingham emigrated and was replaced by Jack Lyness. In 1963 Staff Nurse Kay Maguire (Fig. 8) joined the team and led the nursing developments until her untimely death in 1987. We continued to provide a travelling service when needed, in the RVH Respiratory Intensive Care Unit, in the Mater Hospital's single small room which served for all patients needing intensive care, in the Ulster Hospital, the Craigavon Hospital intensive care unit and even as far as Altnagelvin.



Fig 8. Kathleen (Kay) Maguire, SRN (1935-1987): first staff nurse, later Senior Nursing Officer, Renal Unit, Belfast City Hospital.

By 1964 there were plans for the BCH Tower Block, which was to include a haemodialysis unit. A sketch plan was drawn with the enthusiastic help of Paddy Semple, one of the two architects responsible for the tower block. In 1965 it became clear that some provision for the growing need of the renal unit would be essential long before the most optimistic estimate for the opening of the tower block. Space was not available in the main block and the solution was a new building behind the Ava Hospital. Following the successful treatment of our second chronic haemodialysis patient by renal transplantation in 1965 in St Mary's Hospital in London, we were determined to develop a service for the treatment of chronic renal failure which would include transplantation. We had established Kiil kidney dialysis (more economical in disposable items and did not require priming blood) for four patients with chronic renal failure in 1965, improvising the facilities we lacked. A new patient could be accepted only when an existing one was transferred to London for a transplant. The design of "Renal 1", with differential pressure ventilation allowed good quality reverse barrier nursing, to protect patients from hospital borne infection. This was then thought essential for transplantation as there was then a very high death rate from sepsis of immunosuppressed patients. Death from sepsis was indeed very rare in our subsequent transplant programme. Haemodialysis could be provided in each room, including the transplant suite. A large theatre was equipped for simultaneous dialysis of two chronic renal failure patients.

Until 1968 the medical staff consisted of myself alone. From time to time Professor Bull's British Council Research Fellows came to gain practical

experience in the management of renal failure. From 1962 onwards a succession of British Council Fellows, all from overseas, came to Belfast for the specific purpose of studying the management of renal failure in the Renal Unit. Some stayed long enough to qualify for a PhD. Most returned to their home countries to set up renal services. In 1968, when the first phase of Renal 1 was opened, Dr Soyannwo from Nigeria and Dr Dimtrios Oreopolus from Greece were working in the unit, and both graduated PhD. Oreopolus went to Canada where he later earned world renown for his work on continuous ambulatory peritoneal dialysis (CAPD).⁶

From the early 1970's, haemodialysis was used for the treatment of more and more patients suffering from chronic renal failure. Almost as soon as it opened, the six places for regular dialysis in Renal 1 were insufficient. A new wing was planned to contain 10 haemodialysis beds and ancillary rooms, and opened in 1972. The 30 patients for which Renal 2 was planned soon proved insufficient, and this unit has been reorganised many times to provide treatment for more and more patients. With improved dialysis equipment leading to shorter dialysis time, and use of preparation rooms no longer needed, eventually 178 patients were treated in Renal 2, 55% three times and 45% twice weekly. Renal 1 and Renal 2 were replaced by a new 40-bed unit, the Belfast City Hospital Dialysis Unit, in 1998.

In the late 1960's access to the patient's bloodstream by Scribner's semi-permanent shunt was superseded by the Bresco-Cimino subcutaneous arteriovenous fistula. This technique was brought to Belfast by a young Dublin urological registrar, Sean Hansom, to whom we continue to be grateful. During the late 1970's systems of pumps were devised permitting dialysis by a single needle instead of two, which causes less discomfort to the patient, and sometimes enables the use of a less than ideal AV fistula. The Northern Ireland Kidney Research Fund provided for the special equipment needed in 1978.

This fund had been set up in 1971 by Mrs Josie Kerr and her husband Walter, with the help of other patients, their families and friends. Their devoted work has been of immense help over the years. Most of the present staff of the Nephrology Unit, including Dr James Douglas and Dr Ciaran Doherty, were Northern Ireland Kidney Research

Fund Fellows. Many nephrologists trained in the same way emigrated to posts on the other side of the Atlantic and Europe. Mrs Kerr was later awarded the MBE.

It was known from the end of the 19th century that the peritoneal membrane was semi-permeable, permitting the passage of water and electrolytes from the peritoneal cavity into the bloodstream. From the 1920's experiments in animals and human beings showed that the peritoneal membrane could be used for removal of some substances by dialysis. Peritoneal dialysis can be carried out without special equipment other than a suitable plastic cannula and a modified Y-piece transfusion set, using sterile dialysis fluid. This simple method was used from the early 1960's for treatment of acute renal failure, but was less satisfactory than haemodialysis mainly because of the high risk of peritonitis.

In 1977 Popovich and Nolph in the USA showed that very effective control of uraemia was achieved by continuous peritoneal dialysis, the fluid being changed only four times in the 24 hours.⁵ The patient continued with normal activity, but the method had the disadvantage of a high incidence of peritoneal infection. Oreopolus, now in Toronto, introduced several improvements which led to world-wide acceptance of this method of treatment of chronic renal failure.⁶ The important change was the substitution of plastic bags instead of bottles to contain the dialysis fluid. After the fluid has run in, the bag is rolled up and carried around in an unobtrusive bag at the waist, until needed to collect the spent fluid. It is not detached from the permanent flexible cannula during "dwell time". This CAPD method of self-dialysis can be taught to patients of moderate intelligence in one or two weeks. The high rate of peritoneal infection has fallen to acceptable levels with improvements both in technique and in dialysis sets. Automation can be used for self-treatment allowing reasonable hours of sleep during the night. However, some patients may later require haemodialysis because of failure of the peritoneal membrane to continue to filter efficiently. The use of CAPD has become widespread especially for children and older individuals. In Northern Ireland after a rapid increase over the past decade, the number of CAPD patients seems to have stabilised at about 20% of the total dialysis population although overall the numbers of patients on dialysis treatment continue to increase.

As long ago as 1902, Ullman had demonstrated in Vienna that a kidney transplanted from its normal site to the neck would produce urine, even a kidney taken from another animal or another species. Carrell and others repeated this experiment but found that urine production ceased after a few days. Attempts by Voronoy in the Ukraine about 1933 to transplant cadaver kidneys in the human were unsuccessful. In 1935 a young research worker, George Davis Snell, having chosen mouse genetics as his research subject, joined the Jackson Laboratory at Bar Harbour, Maine. The work at the Jackson Laboratory was centred on transplantable tumours in mice, and it was known that resistance in mice to foreign strains of tumours were genetically determined. Snell created and maintained large numbers of inbred mouse strains and their cogenic lines for his research. Lacking a name to describe these postulated genetic factors he called them "histocompatibility genes" on the suggestion of his neighbour across the hall. Using his inbred mice he was able to define lines which differed from a standard inbred strain by a single histocompatibility gene, by the introduction of a foreign but closely linked gene.⁹ About the same time Peter Gorer, working in Guy's Hospital in London, devised a serological method of identifying antigenic differences between strains, publishing his classic paper "The genetic and antigenetic basis of tumour transplantation" as early as 1937.⁷ Gorer went to work in the Jackson Laboratory in 1946. It turned out that Gorer by serology and Snell by inbred mouse linkage had identified the same locus, H-2. H-2 in the mouse turned out to be the analogue of HLA in the human.

During this time, Billingham, Medawar and Brent in London were studying skin transplantation in rabbits. In 1944 Medawar published his experiments on skin autografts and homografts.⁸ Later in a joint study with Snell they demonstrated that a graft of skin made to an unborn mouse would survive. This experiment led to the concepts of immunological tolerance and enhancement. This was the basis of work on the potential for tolerance and enhancement to contribute to human transplantation, discussed at many meetings of the British Transplantation Society in the 1970's.

Snell continued to work with H-2, identifying new alleles, and it became apparent that H-2 in the mouse was a model of great importance in human transplantation. His last area of research

was the identification of alloantigens on lymphocytes using the chromium labelled cytotoxic test. He continued to work at the Jackson Laboratory for the rest of his life. In 1980, aged 76, he shared the Nobel Prize with Barju Benacerrag and Jean Dausset, for the discovery of the major histocompatibility complex. Sadly, Peter Gorer died early, and did not share in the greatest accolade.

Meantime attempts to transplant kidneys in humans in Boston failed, as did attempts by Küss in Paris using steroid in the earliest attempts at immunosuppression. However it was shown in Boston that in animals skin could be transplanted between litter mates, the transplant not being “recognised” as foreign tissue. This led to the first successful human kidney transplant carried out in 1954 in Boston, by Murray and Merrill between identical twins. Over the next decade transplantation between identical twins was carried out in several centres in Europe and America without evidence of rejection, though some failed for technical reasons. An identical twin transplant carried out in Belfast in 1962 was a technical failure.

Few patients reaching end stage kidney failure have a twin able and willing to provide a kidney. Transplantation between less closely related individuals invariably failed from rejection. Whole body irradiation prevented massive infiltration of the graft with lymphocytes and other inflammatory cells but the patients died from uncontrollable sepsis associated with bone marrow suppression. Attempts to use drugs for immunosuppression were made in animal models. Mercaptopurine was found to prolong graft survival in dogs but was very toxic. Burroughs Wellcome in the New Jersey Laboratories produced a derivative of mercaptopurine, azathioprine, which proved a good immunosuppressive and much less toxic when used for dog kidney grafts by Roy Calne and others in Boston. In 1962 Calne and Murray used azathioprine successfully when a kidney taken from a patient dying during an openheart operation was transplanted into an unrelated individual. In 1962 Goodwin in Boston reported successful treatment of several rejection episodes with steroid in a mother-to-child transplant, though the child finally died from sepsis. Azathioprine combined with steroid became generally accepted as the main immunosuppression for transplantation for over two decades. Both are still in use in

combination with other drugs. In 1976 cyclosporin A, a fungal metabolite was found to be a potent immunosuppressive; others have followed, but there is, as yet, no perfect immunosuppressive. Immunosuppression is a huge topic in itself.

The Belfast transplant programme began in 1968 after the opening of Renal 1. This provided a suitable environment. Dr Joseph McEvoy was appointed second nephrologist; and Mr Stewart Clarke and Mr Joseph Kennedy were appointed each to give two consultant sessions to provide continuous cover for harvesting and transplantation of cadaver kidneys. Dr John Alexander (Fig. 9) and Dr Cecil Hewitt volunteered to provide anaesthesia. Joseph Kennedy and John Alexander continued to take part in the transplant programme until retirement in 1996. Other consultants and trainees have contributed while the service has continued to develop, including Mr Gordon Loughridge, Mr Richard Donaldson, Dr James Douglas and Dr

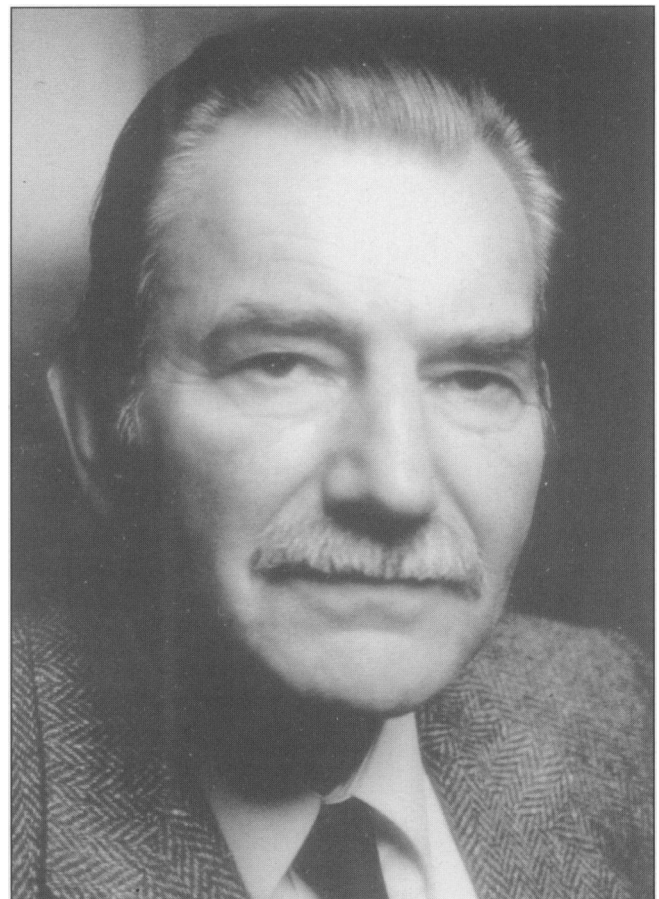


Fig 9. John Alexander, MA, FRCPI, FFARCI, DA (1930–) consultant anaesthetist at the Belfast City Hospital, one of two anaesthetists who formed the first anaesthetist rota for renal transplantation from 1958.

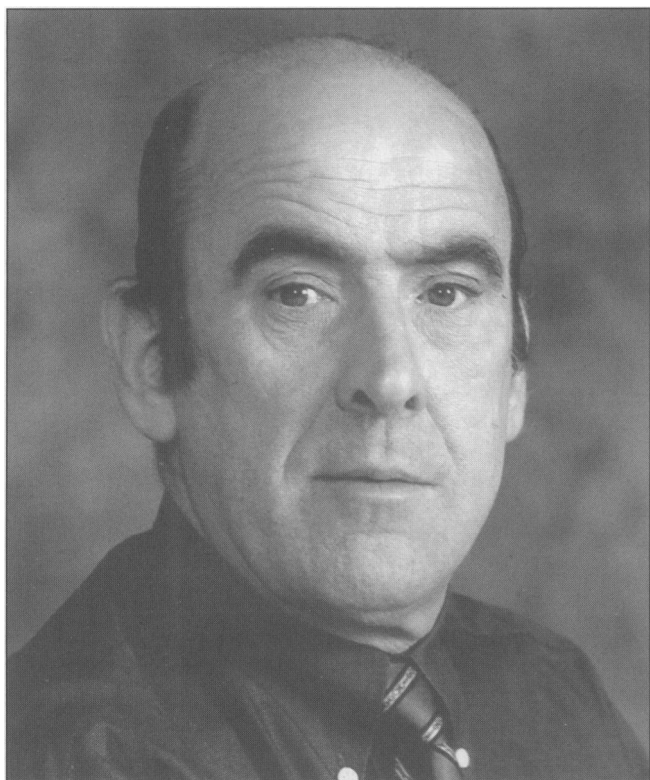


Fig 10. Derek Middleton, BSc, PhD (1946-): Tissue Typing Scientist associated with renal transplantation since 1968.

Ciaran Doherty. Dr Sam Nelson set up the Tissue Typing Service in 1968, later developed by Professor Derek Middleton to gain an international reputation.

The programme was carefully planned, using cadaver kidneys as the main source of grafts. The role of each member of staff was agreed, and each step of the procedure for the removal of cadaver kidneys, their insertion into the recipient, the drugs for immunosuppression and the post-operative care written down to form the "Belfast Recipe for Transplantation".⁹ During the early years all the grafts came from cadavers, later occasional living related donors were used. A significant difference from other centres was the sparing use of corticosteroids. We used much lower doses of steroid, for induction, anti-rejection treatment if needed and long-term maintenance therapy.

The first transplant was carried out on 22nd November 1968. Initially successful it was lost three months later from irreversible rejection. Thereafter we achieved a one year first cadaver graft survival of 80% which was much above the 50% or even less than recorded in many units.



Fig 11. The team responsible for renal replacement therapy for Northern Ireland, with the author.

Back row: Derek Middleton, James Sandford, John Connolly, Robert Kernaghan, Ciaran Doherty, Peter MacNamee, Henry Brown, Peter Maxwell.

Front row: Claire Hill, Peter Garrett, William Nelson, James Douglas, Mary McGeown, Joanne Martin, Maurice Savage, Mary O'Connor.

Our results continued to top the figures collected by the UK Transplant Service until usage of cyclosporin A became general.

By 31st December 1996, 924 transplants had been carried out for 800 patients. Sixty-four came from living donors and 860 from cadavers. The one year first cadaver graft survival continues to hover about 80%, despite many much older and otherwise disadvantaged recipients. I am particularly proud of the long term transplant results; 56% of grafts transplanted more than 10 years ago continue to function.¹⁰

The hope that xenotransplantation may provide organs for transplantation is soundly based on the progress already made to produce transgenic pigs. Certainly progress is being made but there is much to be done before xenotransplantation becomes a clinical tool. It may soon be possible to suppress the initial hyperacute rejection of the transgenic organ, but we do not know whether the kidney's numerous functions will translate unchanged across the species barrier. There is anxiety about pig viral infections proving lethal in humans. Some have expressed ethical concern. I believe that xenotransplantation will become a clinical reality, but that the time may be more distant than some enthusiasts hope.

The future in Belfast is in the hands of the present capable team (Fig. 11). We are happy to welcome a new surgical member of the team, Mr John Connolly, whose brief includes vascular access surgery as well as retrieval of organs and transplantation. The future looks bright for Dublin's renal services. The Beaumont Hospital team has just published an innovative technique on the successful use of kidneys from tiny children for *en bloc* transplantation into adults.¹¹ Dublin teams have already successfully embarked on liver and heart transplantation. Long may the friendship and co-operation continue between Belfast and Dublin, based firmly on our common interests over the years.

ACKNOWLEDGEMENTS

Besides the help of many already mentioned, I gratefully acknowledge the help of the staff of the Robert Gray Regional Respiratory Intensive Care Unit at the Royal Victoria Hospital, and those of many other intensive care units throughout Northern Ireland, who have facilitated the provision of organs for transplantation. We are well

aware of the great increase in their own workload which this imposes. I must again thank the members of the Northern Ireland Kidney Research Fund for their great support over nearly 30 years.

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